Tracking tumor mutations in ctDNA through repetitive plasma samples in patients with newly diagnosed brain cancer - April 2023, AACR Congress, Orlando, US(Abstract)

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INTRODUCTION AND PURPOSE OF THE STUDY

Glioblastoma (GBM) is an aggressive brain cancer with a median overall survival of 16-24 months. Evaluation of treatment effect can be difficult as pseudo progression is seen in approximately 15% of patients. Hence, effective treatment can be stopped prematurily and no approved or standard second line treatment exist. Genomic alterations during treatment can cause treatment resistance and treatment failure. In order to investigate the genomic alterations, consecutive tissue samples are wanted. However, this is often not possible due to risk doing surgery. Therefore, liquid biopsies from plasma, containing circulating cell-free DNA (cfDNA) and circulating cell-free tumor DNA (ctDNA) might be an alternative. Based on findings by our group, we aim to improve treatment evaluation and suggest targeted treatment possibilities by investigating the role of cfDNA and ctDNA in a large prospective cohort, included from a neurooncological out-patient clinic.

MATERIALS AND METHODS

Newly diagnosed patients with GBM, a performance status of 0-1 and planned for concurrent chemo/radiation will be eligible. Whole genome sequencing (WGS) will be done on tissue. Peripheral blood will be collected in cell stabilizing Blood Collection Tubes (STRECK) and cfDNA will be quantified on a Qubit Fluorometer. Samples will be collected before the concurrent treatment and at fixed time points until progression with a total of 8-10 samples per patient. For the ctDNA analyses, a patient specific tumor mutation will be selected based upon WGS data from tumor tissue. The identified mutation will be quantified in plasma (ctDNA) by droplet digital PCR (ddPCR). Dual labeled fluorescent probes for the mutation and the wild type loci will be used and PCR reaction mixtures will be run. Mutant allele fractions (AFs) ≥0.001 (0.1%) will be detected. An increase in ctDNA AF will be recorded if the AF increases from non-detectable to detectable levels (AF ≥ 0.001) or increases in two consecutive samples.

RESULTS

Inclusion began in June 2022 and by time of abstract deadline, we have 27 patients included. Of these, 16 have completed the concurrent setting with a total of five samples per patient. One patient has died and two have progressed. Hence, 24 patients are still on-treatment and sampling and accrual will continue. The first analyses for cfDNA will be run in the winter of 2022/2023 and results will be presented at the conference. CtDNA analyses are planned for autumn 2023.

EXPECTED IMPACT

The expected impacts of this study are specifically in two clinical areas: treatment evaluation and development of new treatment strategies. We aim to

1) find correlation between cfDNA/ctDNA and the clinical course
2) detect a relapse earlier than imaging with MRI and FET/PET analyses
3) aid to diagnose pseudo progression
4) use ctDNA for detection of clonal selection
5) test concordance between mutations detected in tissue and in plasma