

ExTarget– Circulating tumor DNA profiling for response assessment and MRD monitoring in molecular tumor board patients

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Background & objectives

Effective therapies become increasingly available for a variety of patients with solid cancers and potentially targetable genetic alterations. However, treatment responses are often transient due to acquired resistance. Furthermore, because the sensitivity and specificity of radiographic imaging are limited, an accurate and timely assessment of treatment response is suboptimal. Finally, resistance mechanisms to targeted therapies are poorly understood for solid tumors with variants in rare oncogenes (e.g. IDH1, HRAS, NTRK) or under specific treatment regimens (e.g. Enasidenib or TRK inhibitors).

In this project, we will explore the value of circulating tumor DNA (ctDNA) for (i) longitudinal monitoring, (ii) accurate response assessment, and (iii) detection of resistance mechanisms and clonal evolution in patients with solid tumors harboring rare genetic targetable variants.

Methods

We will obtain blood plasma from applicable patients across cooperating EXLIQID Molecular Tumor Boards to facilitate the collection of a meaningful cohort of patients with rare genetic characteristics. We will use targeted capture high-throughput sequencing approaches to both sensitively monitor ctDNA and comprehensively characterize plasma ctDNA with respect to treatment response, after validation of selected assays via ddPCR.

Results

A pilot set of patient samples with variants of interest has been collected, and levels of ctDNA are being explored in the context of the individual treatment situations and contrasted with commonly used disease quantification measures.

Conclusion

Initial insights into the value of ctDNA to explore longitudinal monitoring of rare oncogenic gene variants will be gained.