translational research

DE NOVO MUTATION DETECTION FROM CTDNA CORRELATES WITH VARIANTS DETECTED ON METASTASIS OF PATIENTS WITH ANY KIND OF REFRACTORY CANCER FROM THE SHIVA TRIAL

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Aim: The ability to perform molecular analyses on circulating tumor DNA (ctDNA) is a promising non-invasive tool to determine tumor genomic alterations. Liquid biopsies may provide information when the biopsy is not available, and address tumor heterogeneity. Multiple sampling and ctDNA analysis over time allows identification of emerging predictive biomarkers and collection of pharmacodynamic data. The aim of this study was to assess whether targeted sequencing on ctDNA permits the detection of the same mutations observed on solid tumor from the same patient.

Methods: SHIVA is a multicentric randomized proof-of-concept phase II trial comparing molecularly targeted therapy based on tumor molecular profiling of a mandatory biopsy of a metastatic site versus conventional therapy in patients with any type of refractory cancer (Le Tourneau et al., BJC 2014). The molecular profile within SHIVA is performed on a mandatory biopsy and includes mutation analyses using AmpliSeq cancer panel (Life Technologies). Blood samples for ctDNA analyses are taken before starting treatment, between day 7 and day 15, at first tumor evaluation, and at disease progression. The same approach was applied here to ctDNA before treatment and mutational profiles were compared to those from tumor biopsies. The bioinformatics analysis was done in a blinded manner.

Results: ctDNA analysis was done on 19 patients including 3 patients with tumor biopsy not eligible for analysis. The mutation(s) identified from the solid tumor biopsy was confirmed in all corresponding blood samples (16/16) and 1 mutation was identified de novo in a patient whose tumor biopsy was uninformative. Tumor types included breast (5), lung (3), ovary (2), cervix (2) among others. Median ctDNA amount was 37 ng/mL [range: 7 - 423].

Conclusions: Our results suggest that targeted sequencing of ctDNA across a panel of genes can reliably detect tumor sample mutations de novo without any a priori information from the tumor biopsy. Further analyses on ctDNA from different time points of the patient’s treatment will give more insight into the potential of liquid biopsies to follow up disease progression and response to treatment.

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