Liquit Biopsy using “Cell — Free DNA” as Predictive Marker of Response after Radiotherapy in Solid Tumors

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Purpose/Objective(s): The use of “Liquid biopsy” using circulating cell-free DNA (cfDNA) is gaining importance as predictive marker for monitoring treatment outcome in cancer patients. We investigated the clinical significance of cfDNA monitoring in patients with solid tumors treated with radiotherapy (RT).

Materials/Methods: Twenty patients aged 37-74 yrs (median age 55.5yrs) diagnosed with advanced/ metastatic cancers, on RT were recruited in an IRB-approved prospective study. Blood samples were collected before starting RT (T1), during RT (T2) and 30 and 60 days after RT (T3 and T4 respectively). The cohort comprised of 6 Lung, 4 stomach, 4 cervical and 6 Breast cancer patients. The cfDNA was purified using a QIAamp Circulating Nucleic Acid Kit (Qiagen, Valencia, CA, USA) and quantified and the quality was established using an ALU-based qPCR assay on an AriaMax Real—time PCR System (Agilent, USA).

Results: The cfDNA levels ranged from 1.2-14 ng/mL pre-RT and 2.5-68 ng/mL post RT. Optimal cut-off values for cfDNA were set at 10ng/mL pre-RT and 15ng/mL post RT to stratify patients into low-DNA (LDNA) and high- DNA (HDNA) groups. The pre-RT HDNA in the cohort presented with more advanced and metastatic disease. Quantitative analysis showed that the cfDNA load initially increased significantly post-RT in some patients which correlated with their good treatment outcomes as regression in tumor and disease burden as per the PET-CT scan results. Since, total cfDNA is derived by cell death associated with apoptosis and necrosis, the increase in cfDNA post RT could be due to more cell death indicating good response to RT. This effect was dose - dependent. On follow up after 2-2.5 months post completion of RT, the cfDNA levels reduced significantly with a good outcome. On the contrary, patients not showing any change in the cfDNA load post RT had less response and a progressive disease confirming a poor response to RT.

Conclusion: Since the incidence of congenital anomalies is below 2.5% in the general population, it was concluded that the population of children undergoing CT is completely different from that not undergoing CT. It was reported that children with birth defects had a higher risk of cancer compared with children without birth defects, with a relative risk estimated to be approximately 3.0. The two groups should not be compared.