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Combination of solid and liquid biopsy genomic profiling for tumor heterogeneity characterization

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BACKGROUND

Characterization of inter- and intra-tumor heterogeneity has become a critical issue in the pipeline of personalized medicine. In this context, although liquid biopsy has been recognized as a promising tool to complement, enrich, and monitor patient’s disease [1], we are still at the beginning of incorporating these into routine oncology practice. To this purpose, we evaluate the usefulness of an integrated approach that combines the analysis of both liquid (peripheral blood) and liquid-based solid biopsy samples, with the latter routine.

METHODS

We analyzed 157 samples of metastatic patients, with different cancer types (Table 1), using the OncoSTRAT&GO® solution (OncoDNA SA, Soncevi, Belgium through a distributor in the USA, Spain) that implements Next-Generation Sequencing (NGS) for Tumor Technology 3.0 Technology, combined with additional clinical features (tumor mutational burden (TMB), microsatellite instability (MSI), methylation status of promoter), that allows it to sequence more than 220 genes and evaluate the expression of the high-protein load of tumors in solid and liquid biopsies.

We then applied descriptive statistics, the nonparametric Mann-Whitney inference test was used to get insights on the concordant and discordant VAFs distribution of actionable variants.

RESULTS

We analyzed 157 samples of metastatic patients, with different cancer types (Table 1) using the OncoSTRAT&GO® solution (OncoDNA SA, Soncevi, Belgium through a distributor in the USA, Spain) that implements Next-Generation Sequencing (NGS) for Tumor Technology 3.0 Technology, combined with additional clinical features (tumor mutational burden (TMB), microsatellite instability (MSI), methylation status of promoter), that allows it to sequence more than 220 genes and evaluate the expression of the high-protein load of tumors in solid and liquid biopsies.

Complete concordance of 61.8% was observed between both types of biopsies variants. The rest of samples presented different discordant patterns that could be detected in both solid and liquid biopsies (table 1). A complete molecular profile combination of solid and liquid biopsy genomic profiling for tumor heterogeneity characterization.

For the tumoral methylated status (TMB) analysis, a double blind score was calculated, based on a predefined scoring method, and the consensus of both analyses was used to define the level of expression or activation of the proteins. Different sets of NTCs were performed, depending on the cancer type, with an average number of 10/15 NTC per sample.

Complete concordance, in the tumor type, other biomolecular test performed included either (i) methylation of the MGMT promoter, (ii) immunohistochemistry (IHC) and (iii) microsatellite instability (MSI).

Finally, the complete molecular profile obtained from the combination of NTC analysis, and additional test, allow to explore the possible therapies for each cancer type. In this sense, we carried out a literature search to identify published official guidelines, retrospective and prospective clinical studies pertaining to genomic alterations and their association with outcome for cancer patients. We divided those therapies identified with a potential clinical benefit (Figure 2) according to the drug type: target therapies, hormonal therapy, immunotherapies and cell therapies.

CONCLUSIONS

Our strategy indicates that the combination of solid and liquid biopsies analysis in clinical practice provides additional information in 25% of the cases, discordant markers can guide decisions to the sensibility of the analysis and consequently should be associated to tumor heterogeneity, low tumor burden and/or treatment response. Our results show the usefulness of an integrated approach, combining in a broad characterization of the tumor for a better disease management.

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References

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