Individualized longitudinal tumor-informed ctdna monitoring in advanced cancers using ots-probes dedicated to digital pcr

Abstract Submitter: Satoshi Nishizuka, Japan*

Co-Authors: Hayato Hiraki, Akiko Yashima-Abo, Minit Jain, Taiga Sasaki, Shinji Tamada, Takeshi Iwaya

*Iwate Medical University Institute for Biomedical Sciences

Abstract

Background: Circulating tumor DNA (ctDNA) has demonstrated its ability to reflect tumor burden. Although digital PCR (dPCR) is a highly sensitive and cost-effective method for frequent ctDNA monitoring, its implementation has been hindered by the lack of readily available individualized primer/probe sets. To address this, we developed a dPCR primer/probe library (OTS-Probes) specifically designed for an individualized longitudinal tumor-informed ctDNA monitoring system called OTS-Assay.

Objective: To evaluate clinical validity and utility of the OTS-Assay.

Methods: OTS-Assay includes the following three steps: (a) “OTS-Scan” - A panel sequencing to identify patient tumor-unique somatic mutations; (b) “OTS-Select” - An automated program that selects optimal mutations for ctDNA monitoring; and (c) “OTS-Monitor” - A system that quantifies variant allele frequency (VAF) in ctDNA. VAF was calculated at each time point to generate longitudinal ctDNA dynamics. These data were analyzed in conjunction with clinical information in both observational and interventional prospective studies.

Results: OTS-Assay was performed for 23 advanced cancers. A strong correlation (r = 0.94) was observed between VAFs obtained from NGS and dPCR (n=503). However, VAFs from dPCR tended to show true greater variability at lower levels compared to NGS. Individualized longitudinal ctDNA monitoring during treatment revealed that nearly 90% of VAFs were below 1%, with post-treatment VAFs significantly lower than pre-treatment levels (n=3,245). The clinical validity of the OTS-Assay was assessed based on its ability to provide insights into early relapse prediction, treatment efficacy evaluation, and no relapse corroboration. The assay demonstrated the clinical validity in 80-90% gastrointestinal cancers (n=151). Interestingly, while ctDNA monitoring provided valuable insights across tumor types, median VAFs in glioblastoma patients (n=11) were 10-fold lower than in other solid tumors (n=229). Regarding treatment response, VAFs during chemotherapy showed good consistency with RECIST criteria (n=27), while ICI treatment showed some discrepancies (n=39). An interim analysis of a prospective interventional study in advanced esophageal carcinoma suggested that therapeutic intervention based on ctDNA monitoring was associated with a trend toward improved survival compared to conventional imaging-based treatment strategies.

Conclusion: The OTS-Assay demonstrates meaningful clinical validity and utility as a tool for individualized longitudinal ctDNA monitoring in advanced cancers.

Do you have any conflicts of interest?

Yes, I have a conflict of interest.

SN is CEO of Quantdetect, Inc.