Mutation Detected
In FFPE tumor:
c.34G>T; p.G12C

Patient of Plasma
4.0 mL
1.0 mL
3.0 mL

METHODS

Oncogenic mutations confer a survival and growth advantage to cancer cells
Identifying oncogenic mutations in cancer can provide druggable targets for cancer therapies
Plasma cell-free (cf) DNA in individuals with cancer offers an easily obtainable, low-risk, and inexpensive source of material for mutation analysis
Longitudinal assessment of cfDNA can be used for monitoring of molecular changes throughout cancer therapy.

METHODS

Patients with advanced cancers, who were previously tested for BRAF V600 (42), KRAS G12/G13 (43), or both mutations (1) in the tumor samples (primary or metastatic) in a CLIA-certified laboratory during their clinical care were prospectively enrolled.
DNA from plasma (3-4ml) from patients with advanced cancers who progressed on systemic therapy were tested for BRAF V600 and KRAS G12 and G13 mutations using the ICE COLD-PCR platform
ICE COLD-PCR, “Improved and Complete Enrichment CClassification at Lower Denaturation” selectively amplifies mutant DNA by exploiting differences in denaturation temperatures between mutant DNA duplexes and normal “wild type” DNA duplexes
KRAS Exon 2 and BRAF Exon 15 ICE COLD-PCR was performed on plasma samples
Amplicons were analyzed by Sanger sequencing

RESULTS

Plasma Volume for Robust Mutation Detection

Concordance Analysis: cfDNA vs. tissue

Longitudinal Assessment of cfDNA Mutations

Patient 45: Metastatic Melanoma with BRAF V600E Mutation

Patient 22: Metastatic Melanoma with BRAF V600E Mutation

Patient Characteristics

BRAF mutations

KRAS mutations

Patient 14: Metastatic Appendiceal Carcinoma with BRAF V600E Mutation

RESULTS

TABLE

BACKGROUND

Oncogenic mutations confer a survival and growth advantage to cancer cells
Identifying oncogenic mutations in cancer can provide druggable targets for cancer therapies
Plasma cell-free (cf) DNA in individuals with cancer offers an easily obtainable, low-risk, and inexpensive source of material for mutation analysis
Longitudinal assessment of cfDNA can be used for monitoring of molecular changes throughout cancer therapy.

RESULTS

BRAF and KRAS Mutation Testing in Plasma Cell-Free DNA with ICE COLD-PCR in Patients with Advanced Cancers

BRAF and KRAS mutations were prospectively tested in plasma samples from patients with advanced cancers who progressed on systemic therapy. BRAF and KRAS mutations were determined in a CLIA-certified laboratory during their clinical care.

RESULTS

BRAF mutations

KRAS mutations

Patient Characteristics

BRAF mutations

KRAS mutations

Patient 18: Metastatic Sigmoid Cancer with KRAS G13D Mutation

RESULTS

BRAF mutations

KRAS mutations

CONCLUSIONS

ICE COLD-PCR detection of actionable mutations in BRAF and KRAS in cfDNA from plasma of patients with advanced cancers is feasible with an acceptable level of concordance with mutation testing of tumor tissue in the CLIA laboratory
Longitudinal assessment of cfDNA mutations can demonstrate changes in mutation status during therapy, which seem to be in agreement with clinical course

Patient 14: Metastatic Appendiceal Carcinoma with BRAF V600E Mutation

Patient 22: Metastatic Melanoma with BRAF V600E Mutation

Patient 45: Metastatic Melanoma with BRAF V600E Mutation

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