SPACEWALK: Plasma NGS for remote evaluation of ALK drug resistance in advanced NSCLC

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Background

- Precision therapy for cancer drug resistance requires detection of resistance mutations and treatment with appropriate targeted therapies.
- This paradigm is well established in EGFR-mutant NSCLC®, yet our understanding of drug resistance in ALK-positive NSCLC is more limited.
- Next-generation sequencing (NGS) of plasma free cell DNA (cfDNA) now permits noninvasive interrogation of drug resistance.
- To facilitate improved understanding of ALK drug resistance and the effectiveness of treatment strategies, we launched this remote participation study (NCT0333934).

Methods

- The SPACEWALK [Study of Plasma next generation sequencing for remote Assessment, Patient enrollment and participation remotely to permitting a larger cohort of patients with ALK-drug resistance] study offers plasma NGS with appropriate targeted therapies.
- This paradigm is well established in NSCLC for next-gen ALK & systemic TKIs using plasma NGS.
- Patients consent, enroll and participate remotely to permitting a larger cohort of patients with ALK drug resistance.
- Remote phlebotomists can be dispatched to the patient’s home when necessary to ease the burden of participation.
- Blood is sent to Resolution Bioscience (Kirkland, WA) for cfDNA extraction and hybrid capture (100).

Result

- Of the 56 returned results, the known ALK fusion was detected in 25 (45%) with a median ALK fusion AF of 2.9% (range 0.1%-3.7%).
- Of the 25 patients with an ALK fusion detected, 13 (52%) showed a reduction in the ALK fusion AF. No somatic ALK mutations were seen in the absence of a detected fusion.
- 6 patients had a MET amplification detected with a median of 8 copies (range 2-22).
- 1 patient had a KRAS G12V mutation detected at 10% AF.

Discussion

- Remote-participation studies like SPACEWALK may offer a new mechanism for characterizing resistance to emerging targeted therapies in rare cancer populations.
- Plasma NGS permits the detection of targetable resistance mechanisms in patients with ALK-positive NSCLC and drug resistance.
- However, robustness of different plasma NGS assays for ALK fusions varies, and further assay optimization may be needed.
- Repeat analysis of plasma cfDNA on therapy offers a noninvasive method for capturing treatment effect.

References

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