Tumor Board Tuesday – Dr. Balazs Halmos & Dr. Angelica D'Aiello, 03/07/2023:
ctDNA: Utility in NSCLC

Posttest Rationale

1. **What would you do next for 80yo neversmoker with path-confirmed mSCC, TPS 1%, a R lung mass and a R femoral lytic lesion who undergoes R ORIF?**

    a. chemo/IO
    b. ctDNA for NGS
    c. Lung/nodal biopsy for NGS
    d. Wallet biopsy

Rationale: NGS testing of ctDNA is likely the best choice for this patient - approximately 10.5% of patients with SCC have actionable alterations, though the guidelines recommend only consideration of molecular testing in this patient population. Testing of ctDNA can be a useful complement to tissue-based testing and is largely consistent with known tissue-profiling landscape, has a high TAT and concordance rate, is minimally invasive, and better captures tumor heterogeneity.A bone biopsy, on the other hand, can be challenging for NGS testing, and a new lung biopsy will take a significant amount of time.

Reference: Lam VK, Tran HT, Banks KC, et al. Targeted Tissue and Cell-Free Tumor DNA Sequencing of Advanced Lung Squamous-Cell Carcinoma Reveals Clinically Significant Prevalence of Actionable Alterations. Clin Lung Cancer. 2019;20(1):30-36 e3. doi:10.1016/j.cllc.2018.08.020

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Non-Small Cell Lung Cancer (v2.2023). Updated February 17, 2023. Accessed March 6, 2023. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

Rolfo C, Mack P, Scagliotti GV, et al. Liquid Biopsy for Advanced NSCLC: A Consensus Statement From the International Association for the Study of Lung Cancer. J Thorac Oncol. 2021;16(10):1647-1662. doi:10.1016/j.jtho.2021.06.017

2. **What is the most likely cause of discordant findings between ctDNA and tissue mol testing in a pt with path-confirmed local NSCLC recurrence following definitive RT with pos EGFR Exon 19 del on tissue bx, but ctDNA which shows only ATM G1016R mutation (VAF 0.1%)?**

    a. False pos ATMm on ctDNA
    b. False neg EGFRm on ctDNA
    c. False neg ATMm on tissue
    d. False pos EGFRm on tissue

Rationale: The most likely cause of these results is a false negative from the ctDNA NGS - ie, the EGFR exon 19 deletion was not detected in the ctDNA sample.

Reference: Abbosh C, Birkbak NJ, Wilson GA, et al. Phylogenetic ctDNA analysis depicts early-stage lung cancer evolution. Nature. 2017;545(7655):446-451. doi:10.1038/nature22364